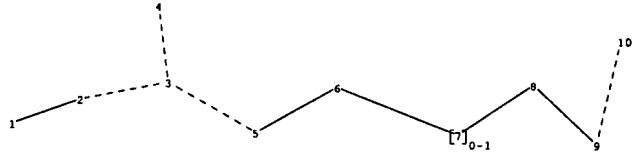
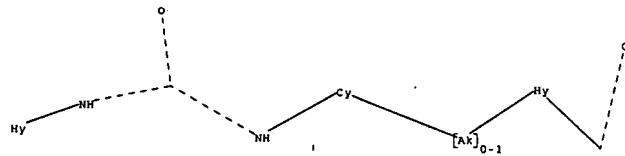


EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|-------|------|--|-----------------|------------------|---------|------------------|
| L1 | 3870 | ((544/336) or (514/338) or (546/271.7) or (546/277.1) or (514/338) or (546/275.7) or (544/353) or (514/338)).CCLS. | US-PGPUB; USPAT | OR | OFF | 2007/11/13 10:54 |
| L2 | 245 | 1 and cancer and urea | US-PGPUB; USPAT | OR | OFF | 2007/11/13 10:54 |



chain nodes :

1 2 3 4 5 6 7 8 9 10

chain bonds :

1-2 2-3 3-4 3-5 5-6 6-7 7-8 8-9 9-10

exact/norm bonds :

1-2 2-3 3-4 3-5 5-6 6-7 7-8 8-9 9-10

Match level :

1:Atom 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:Atom 7:CLASS 8:Atom 9:CLASS 10:CLASS

Generic attributes :

1:
Type of Ring System : Polycyclic
8:
Saturation : Unsaturated

Element Count :

Node 8: Limited
C,C5
N,N1

10788426

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PASSWORD :

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 3 JUL 02 SCISEARCH enhanced with complete author names

NEWS 4 JUL 02 CHEMCATS accession numbers revised

NEWS 5 JUL 02 CA/CAplus enhanced with utility model patents from China

NEWS 6 JUL 16 CAplus enhanced with French and German abstracts

NEWS 7 JUL 18 CA/CAplus patent coverage enhanced

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NEWS 9 JUL 30 USGENE now available on STN

NEWS 10 AUG 06 CAS REGISTRY enhanced with new experimental property tags

NEWS 11 AUG 06 FSTA enhanced with new thesaurus edition

NEWS 12 AUG 13 CA/CAplus enhanced with additional kind codes for granted patents

NEWS 13 AUG 20 CA/CAplus enhanced with CAS indexing in pre-1907 records

NEWS 14 AUG 27 Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB

NEWS 15 AUG 27 USPATOLD now available on STN

NEWS 16 AUG 28 CAS REGISTRY enhanced with additional experimental spectral property data

NEWS 17 SEP 07 STN AnaVist, Version 2.0, now available with Derwent World Patents Index

NEWS 18 SEP 13 FORIS renamed to SOFIS

NEWS 19 SEP 13 INPADOCDB enhanced with monthly SDI frequency

NEWS 20 SEP 17 CA/CAplus enhanced with printed CA page images from 1967-1998

NEWS 21 SEP 17 CAplus coverage extended to include traditional medicine patents

NEWS 22 SEP 24 EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS 23 OCT 02 CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt

NEWS 24 OCT 19 BEILSTEIN updated with new compounds

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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STRUCTURE FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5
DICTIONARY FILE UPDATES: 12 NOV 2007 HIGHEST RN 953132-99-5

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>
Uploading C:\Documents and Settings\brobins01\My
Documents\stnweb\Queries\asdfdsa.str

L1 STRUCTURE UPLOADED

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L1 HAS NO ANSWERS
L1                      STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
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Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 34918 TO ITERATE

5.7% PROCESSED 2000 ITERATIONS 0 ANSWERS

Updated Search

10788426

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 687191 TO 709529
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

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DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:Y
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FULL SCREEN SEARCH COMPLETED - 700701 TO ITERATE

100.0% PROCESSED 700701 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.12

L3 3 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 174.35 174.56

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FILE COVERS 1907 - 13 Nov 2007 VOL 147 ISS 21
FILE LAST UPDATED: 12 Nov 2007 (20071112/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 2 L3

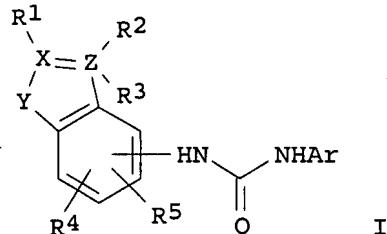
=> d 14, ibib abs hitstr, 1-2

L4 ANSWER 1 OF 2 HCPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:591913 HCPLUS
DOCUMENT NUMBER: 137:150215
TITLE: Cdk4 and/or Cdk6 inhibitors with biaryl ureas and

Updated Search

their salts as antitumor agents
 INVENTOR(S): Hatayama, Satoshi; Hayashi, Kyoko; Honma, Mitsuki;
 Takahashi, Ikuko
 PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 194 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------------------|----------|-----------------|----------|
| JP 2002220338 | A | 20020809 | JP 2001-18755 | 20010126 |
| PRIORITY APPLN. INFO.: | | | JP 2001-18755 | 20010126 |
| OTHER SOURCE(S): | MARPAT 137:150215 | | | |
| GI | | | | |

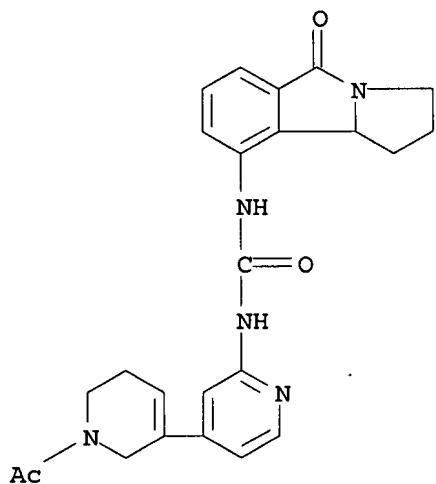


AB This invention relates to the general structures (I; Ar = N-containing hetero aromatic ring, X, Z = C, etc.; Y = CO, etc.; R1-R5 = H, etc.) and their salts as Cdk4 and/or Cdk6 inhibitors. I have antiproliferative effects on cancer cells and are potential antitumor agents. Formulation examples of I capsules, tablets, and injections were given.

IT 322685-53-0 445430-92-2
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Cdk4 and/or Cdk6 inhibitors with biaryl ureas and their salts as antitumor agents)

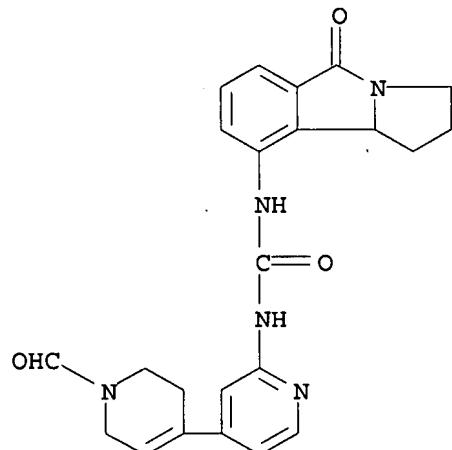
RN 322685-53-0 HCAPLUS

CN 3,4'-Bipyridine, 1-acetyl-1,2,5,6-tetrahydro-2'-[[[(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 445430-92-2 HCAPLUS

CN Urea, N-(1'-formyl-1',2',3',6'-tetrahydro[4,4'-bipyridin]-2-yl)-N'-(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl) - (CA INDEX NAME)



L4 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:78363 HCAPLUS

DOCUMENT NUMBER: 134:147614

TITLE: Preparation of N,N'-biarylurea derivatives as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6)

INVENTOR(S): Hayama, Takashi; Hayashi, Kyoko; Honma, Mitsutaka; Takahashi, Ikuko

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 460 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

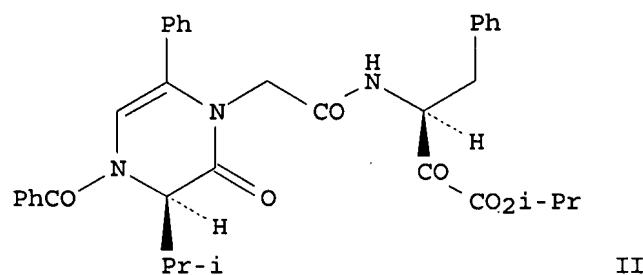
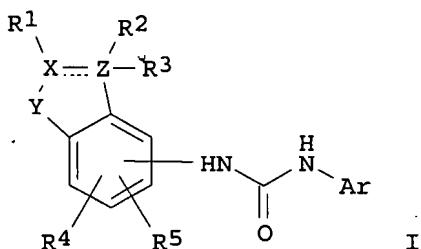
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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| WO 2001007411 | A1 | 20010201 | WO 2000-JP4991 | 20000726 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2380389 | A1 | 20010201 | CA 2000-2380389 | 20000726 |
| JP 2001106673 | A | 20010417 | JP 2000-274175 | 20000726 |
| EP 1199306 | A1 | 20020424 | EP 2000-949909 | 20000726 |
| EP 1199306 | B1 | 20051207 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| EP 1557168 | A2 | 20050727 | EP 2005-101402 | 20000726 |
| EP 1557168 | A3 | 20070523 | | |
| R: DE, ES, FR, GB, IT | | | | |
| ES 2251395 | T3 | 20060501 | ES 2000-949909 | 20000726 |
| US 6958333 | B1 | 20051025 | US 2002-31795 | 20020402 |
| US 2007027147 | A1 | 20070201 | US 2004-2422 | 20041203 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | JP 1999-211384 | A 19990726 |
| | | | EP 2000-949909 | A3 20000726 |
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| | | | US 2002-31795 | A3 20020402 |

OTHER SOURCE(S): MARPAT 134:147614
GI

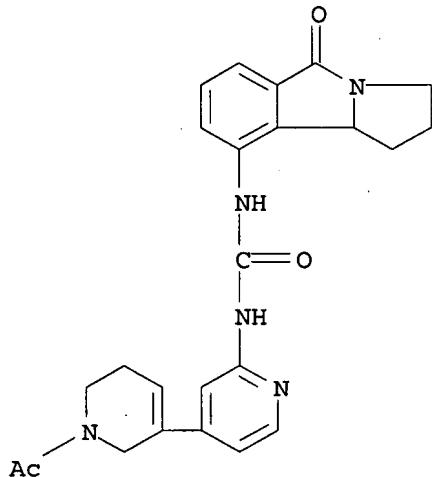


AB N-(hetero)aryl-N'-heterocyclurea derivs. represented by general formula (I) [wherein Ar represents a nitrogenous heterocyclic aromatic group such as (un)substituted pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, pyrrolyl, imidazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, benzothiazolyl, or

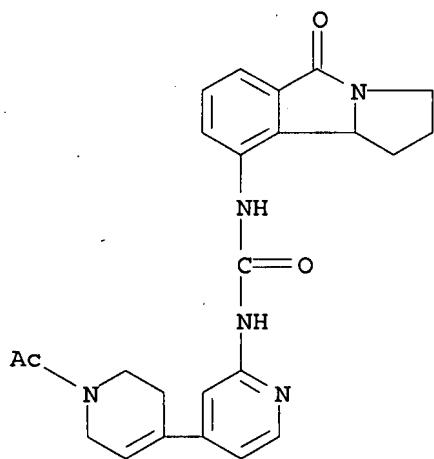
benzoxazolyl; X and Z each represents C or N or together with R1 or R2 and/or R3 represent CH or N; Y represents CO, SO, or SO2; R1 represents hydrogen, (un)substituted lower alkyl, Y3-W2-Y4-R5, etc.; wherein R5 = H, (un)substituted lower alkyl, lower alkenyl, lower alkynyl, lower cycloalkyl, aryl, imidazolyl; isoxazolyl, isoquinolyl, isoindolyl, indazolyl, indolyl, indolidinyl, isothiazolyl, ethylenedioxyphenyl, oxazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, quinoxalinyl, quinolyl, etc.; W2 = ingle bond, O, S, SO, SO2, N-(un)substituted NH, SO2NH, NHSO2NH, NHSO2, CONH, NHCO, NHCONH, NHCO2, etc.; Y3, Y4 = single bond, linear or branched lower alkylene; R2 and R3 each represents hydrogen, lower alkyl or alkoxy, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above), or one of R2 and R3 together with R1 and X forms cyclohexane, cyclopentane, piperidine, 3,4,5,6-tetrahydro-1,3-oxazine, tetrahydrothiopyran, pyrrolidine, tetrahydrothiophuran, oxazolidine ring, etc.; R4 and R5 represent H, halo, OH, amino, or Y3-W2-Y4-R5 (Y3, W2, Y4, R5 = same as above)] or salts thereof are prepared. The compds. (e.g. II) have a remarkable proliferation-inhibitory effect on tumor cells. A Cdk4 and/or Cdk6 inhibitor for use in the therapy of malignant tumor can hence be provided. II showed IC50 of 0.061 and 0.019 μ M against cyclin-D1-Cdk4 and cyclin-D2-Cdk4, resp., vs. 0.36 and 0.056 μ M, resp., for (\pm)-flavopiridol, and inhibited the proliferation of HCT116 and MKN-1 cells with IC50 of 0.013 and 0.10 μ M, resp., vs. 0.15 and 0.87 μ M, resp., for (\pm)-flavopiridol. Pharmaceutical formulations containing I were prepared.

IT 322685-53-0P 322685-55-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of N-(hetero)aryl-N'-heterocyclurea derivs. as inhibitors of cyclin-dependent kinases (Cdk4 and Cdk6) and antitumor agents)

RN 322685-53-0 HCAPLUS
 CN 3,4'-Bipyridine, 1-acetyl-1,2,5,6-tetrahydro-2'-[[[(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 322685-55-2 HCAPLUS
 CN 4,4'-Bipyridine, 1-acetyl-1,2,3,6-tetrahydro-2'-[[[(2,3,5,9b-tetrahydro-5-oxo-1H-pyrrolo[2,1-a]isoindol-9-yl)amino]carbonyl]amino]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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| | ENTRY | SESSION | |
| FULL ESTIMATED COST | 13.14 | 187.70 | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| CA SUBSCRIBER PRICE | -1.56 | -1.56 | |

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 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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10788426

L1 STRUCTURE UPLOADED
L2 0 S L1
L3 3 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 10:25:56 ON 13 NOV 2007
L4 2 S L3

FILE 'CAOLD' ENTERED AT 10:26:12 ON 13 NOV 2007

=> s 13
L5 0 L3

=> file hcaplus
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ENTRY SESSION
FULL ESTIMATED COST. 0.45 188.15

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
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CA SUBSCRIBER PRICE 0.00 -1.56

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FILE LAST UPDATED: 12 Nov 2007 (20071112/ED)

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L2 0 S L1
L3 3 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 10:25:56 ON 13 NOV 2007
L4 2 S L3

FILE 'CAOLD' ENTERED AT 10:26:12 ON 13 NOV 2007
L5 0 S L3

Updated Search

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=> s dumas, j?/au and boyer, s?/au and verma, s?/au and adnane, l?/au and chen, y?/au and lee, w?/au and phillips, b?/au and smith, r?/au and scott, w?/au and burke, j?/au and chen, z?/au

766 DUMAS, J?/AU
 325 BOYER, S?/AU
 1697 VERMA, S?/AU
 10 ADNANE, L?/AU
 47778 CHEN, Y?/AU
 13759 LEE, W?/AU
 1030 PHILLIPS, B?/AU
 15581 SMITH, R?/AU
 2111 SCOTT, W?/AU
 2095 BURKE, J?/AU
 25681 CHEN, Z?/AU

L6 1 DUMAS, J?/AU AND BOYER, S?/AU AND VERMA, S?/AU AND ADNANE, L?/AU
 AND CHEN, Y?/AU AND LEE, W?/AU AND PHILLIPS, B?/AU AND SMITH,
 R?/AU AND SCOTT, W?/AU AND BURKE, J?/AU AND CHEN, Z?/AU

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L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:756711 HCAPLUS

DOCUMENT NUMBER: 141:277641

TITLE: Preparation of bicyclic (hetero)aryl- and
 pyridine-containing diaryl ureas as Raf kinase and
 angiogenesis inhibitors useful in the treatment of
 cancer and other disorders

INVENTOR(S): Dumas, Jacques; Boyer, Stephen;
 Verma, Sharad; Adnane, Lila;
 Chen, Yuanwei; Lee, Wendy;
 Phillips, Barton; Smith, Roger A.;
 Scott, William J.; Burke, Jennifer;
 Chen, Jianqing; Chen, Zhi; Fan, Jianmei;
 Miranda, Karl; Raudenbush, Brian; Redman, Aniko; Shao,
 Jianxing; Su, Ning; Wang, Gan; Yi, Lin; Zhu, Qingming
 Bayer Pharmaceuticals Corporation, USA

PATENT ASSIGNEE(S):

SOURCE: PCT Int. Appl., 162 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

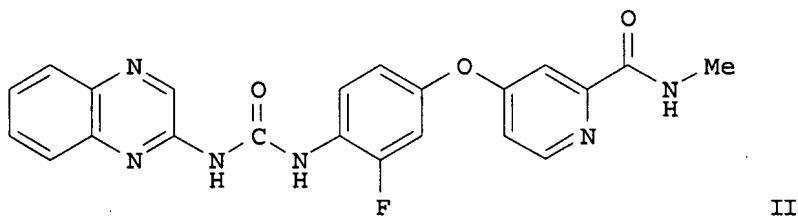
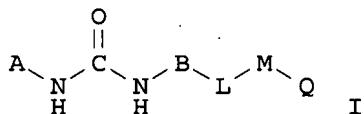
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|---|----------|-----------------|----------|
| WO 2004078748 | A2 | 20040916 | WO 2004-US6287 | 20040301 |
| WO 2004078748 | A3 | 20041111 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2516931 | A1 | 20040916 | CA 2004-2516931 | 20040301 |

10788426

| | | | | |
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| EP 1608639 | A2 | 20051228 | EP 2004-716166 | 20040301 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2006519265 | T | 20060824 | JP 2006-508978 | 20040301 |
| MX 2005PA09104 | A | 20060531 | MX 2005-PA9104 | 20050826 |
| PRIORITY APPLN. INFO.: | | | | |
| US 2003-450348P P 20030228 | | | | |
| WO 2004-US6287 W 20040301 | | | | |

OTHER SOURCE(S): MARPAT 141:277641
GI



AB Title compds. I [wherein A = benzimidazolyl, 2,3-dihydro-1H-indolyl, 2,3-dihydro-1H-indenyl, 1H- or 2H-indazolyl, 1,3-benzodioxin-6-yl, quinoxalinyl, etc.; B = (un)substituted Ph, naphthyl, pyridinyl, quinolinyl; L = (CH₂)_m-D-(CH₂)_n; m, n = independently 0-4; D = O, C(:O), NH and derivs., NHCO and derivs., S, CONH and derivs.; M = (un)substituted pyridine ring; Q = C(:O)H and derivs., CO₂H and derivs., CONH₂ and derivs.; and their pharmaceutically acceptable salts, prodrugs, and metabolites] were prepared as Raf kinase inhibitors for treating hyper-proliferative and angiogenesis disorders, alone or in combination with cytotoxic therapies. For example, urea II was prepared from 4-(4-Amino-3-fluorophenoxy)-N-methylpyridine-2-carboxamide (preparation given), triphosgene, 2-aminoquinoxaline, in the presence of DIPEA/anhydrous DMF at 75°. Selected I showed 80% inhibition of c-Raf kinase at 1 μM. Thus, I are useful for treating cancer and other Raf kinase-mediated diseases.